

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 50-746**

**CHEMISTRY REVIEW(S)**

# DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS

Review of Chemistry, Manufacturing and Controls

**NDA #:** 50-746    **CHEM.REVIEW #:** 1    **REVIEW DATE:** 11/24/97

## SUBMISSION/TYPE    DOCUMENT DATE    CDER DATE    ASSIGNED DATE

ORIGINAL	12-12-96	12-12-96	2-29-97
AMENDMENT(BC)	7-21-97	7-23-97	7-29-97
AMENDMENT(NC)	7-23-97	7-24-97	7-29-97
AMENDMENT(BC)	10-01-97	10-02-97	10-06-97
AMENDMENT(BC)	10-29-97	10-30-97	11-06-97
AMENDMENT(BP)	11-04-97	11-04-97	11-12-97
AMENDMENT(BC)	11-21-97	11-21-97	11-24-97

## NAME & ADDRESS OF APPLICANT

SmithKline Beecham Pharmaceuticals  
One Franklin Plaza  
P.O. Box 7929  
Philadelphia, PA 19101-7929  
(215) 751-3868

## CONTACT

Debra Hackett,  
Manager, U.S. Regulatory Affairs  
(215) 751-3868

## DRUG PRODUCT NAME

Proprietary: Bactroban® Cream, 2%  
Established: Mupirocin calcium cream  
Laboratory Code Name: BRL 4910F (mupirocin calcium dihydrate)  
Chemical type: 3 S

**PHARMACOLOGICAL CATEGORY/INDICATION:** Antibacterial;  
treatment of secondary infected traumatic skin lesions

**DOSAGE FORM:** Topical cream

**STRENGTHS:** 2%w/w mupirocin calcium, 15 and 30g tubes

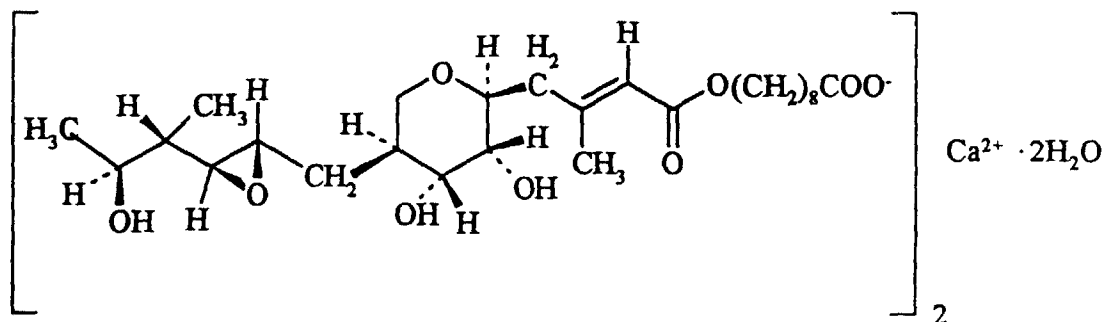
**ROUTE OF ADMINISTRATION:** Topical

**DISPENSED:**                      XX Rx                           OTC

## CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT

Mupirocin calcium dihydrate,  $C_{52}H_{86}O_{18}Ca \cdot 2H_2O$ ; 1075.3 (mupirocin calcium dihydrate) 500.6 (mupirocin free acid);

( $\alpha$  E, 2S,3R,4R,5S)-5-(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]-tetrahydro-3,4-dihydroxy  $\beta$ -methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid, calcium salt (2:1), dihydrate



CAS No. 12650-69-0 (free acid); 115074-43-6 (mupirocin calcium (2:1) dihydrate); 104486-81-9 (mupirocin calcium anhydrous).

#### SUPPORTING DOCUMENTS

IND

DMF

, DMF

DMF

DMF

#### RELATED DOCUMENTS

NDA 50-591; NDA 50-703

#### CONSULTS

1) The establishment inspections have an overall acceptable recommendation (Appendix A). , finished dosage ID tester, was found unacceptable and form 483 issued. The applicant has withdrawn the facility (Amendment dated 11/21/97) and proposed for replacement. The other sites found acceptable include finished dosage packager, DPT Laboratories Inc., finished dosage manufacturer, in San Antonio, TX; Lancaster Laboratories Inc., finished dosage release tester, in drug substance micronizer, in Kent, UK; SmithKline Beecham, finished dosage stability tester and drug substance micronizer, in Crawley, UK; SmithKline Beecham, drug substance manufacturer, in Worthing, UK. A current acceptable inspection report is included in the Appendix

Complete

2) Methods Validations consult have been presented to district are not complete.

Incomplete

3) A trademark consult was submitted for suitability to the Labeling and

Nomenclature Committee ( Dan Boring, Chair 4/21/97). The trademark consult did not find any concerns contrary to the use of the name Bactroban® Cream.

**Complete**

4) A consult for environmental assessment (AEA) was prepared by reviewer and submitted to Nancy Sager, Environmental Scientist, CDER. A finding of no significant impact to the environment was concluded and a FONSI statement is attached to the review.

**Complete**

5) A microbiology sterility consult of the CMC was not initiated.

**REMARKS/COMMENTS:**

The CMC details regarding the drug substance were referenced to the supporting NDA 50-591 and NDA 50-703 for review. Information therefore about the drug substance included in this review comes from the previously approved NDA's and their current Annual Reports.

**CONCLUSIONS & RECOMMENDATIONS:** Approvable

Recommend approval with regard to chemistry, manufacturing and controls. Pending items are method validations and commitments listed on page 44 of this review, as well as satisfactory toxicological evaluation of the two major degradation products.

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M. J. Sloan, Ph. D. Review Chemist

cc: Org. NDA 50-746  
HFD-520/Division File  
HFD-520/DKatague/Team Leader  
HFD-520/Sloan/Chem  
HFD-520/Peters/Pharm  
HFD-520/King/Micro  
HFD-520/Bostwick/MO  
HFD-520/Bell/Stat  
HFD-520/Ajayi/Biopharm  
HFD-520/JBona/CSO  
HFD-830/C-wChen/ONDCIII/Div.Dir.

11/25/97